ORIGINAL ARTICLE

Epidemiology of neonatal group B streptococcal disease in the Netherlands before and after introduction of guidelines for prevention

M Trijbels-Smeulders, G A de Jonge, P C M Pasker-de Jong, L J Gerards, A H Adriaanse, R A van Lingen, L A A Kollée

Arch Dis Child Fetal Neonatal Ed 2007;**92**:F271–F276. doi: 10.1136/adc.2005.088799

See end of article for authors' affiliations

Correspondence to: Dr M Trijbels-Smeulders, University Medical Centre Nijmegen, Department of Paediatrics, PO Box 9101, 6500 HB Nijmegen, the Netherlands; Trijbels@planet.nl

Accepted 12 December 2006
Published Online First 16 January 2007

Objectives: (1) To describe the epidemiology of neonatal group B streptococcal (GBS) disease over five years (1997–2001) in the Netherlands, stratified for proven and probable sepsis and for very early (<12 h), late early (12 h – <7 days) and late (7–90 days) onset sepsis. (2) To evaluate the effect of the introduction in January 1999 of guidelines for prevention of early onset GBS disease based on risk factors.
Methods: Data on cases were collected in collaboration with the Dutch Paediatric Surveillance Unit and corrected for under-reporting by the capture-recapture technique.
Results: Total incidence of proven very early onset, late early onset and late onset GBS sepsis was 0.32, 0.11 and 0.14 per 1000 live births, respectively, and of probable very early onset, late early onset and late onset GBS sepsis was 1.10, 0.18 and 0.02 per 1000 live births, respectively. Maternal risk factors were absent in 46% of the proven early onset cases. Considerably more infants with proven GBS sepsis were boys. 64% of the infants with proven very early onset GBS sepsis were first borns compared with 47% in the general population. After the introduction of guidelines the incidence of proven early onset sepsis decreased considerably from 0.54 per 1000 live births in 1997–8 to 0.36 per 1000 live births in 1999–2001. However, there was no decrease in the incidence of meningitis and the case fatality rate in the first week of life. The incidence of late onset sepsis also remained unchanged.
Conclusion: After the introduction prevention guidelines based on risk factors there has been a limited decrease in the incidence of proven early onset GBS sepsis in the Netherlands. This study therefore recommends changing the Dutch GBS prevention guidelines.

Early onset group B streptococcal (GBS) infection can be prevented by intrapartum antibiotic prophylaxis.[1] In Europe, prevention strategies for this disease were developed later than in the USA.[2] In 1996, the Centers for Disease Control and Prevention (Atlanta, Georgia, USA) recommended guidelines based on one of two strategies.[3] The first strategy consisted of universal screening for GBS colonisation. It was calculated that this strategy would result in intrapartum chemoprophylaxis for 26.7% of all pregnant women and prevent nearly 90% of neonatal cases. The second strategy was based on the presence of risk factors, and with this strategy 18% of all pregnant women would receive intrapartum chemoprophylaxis and 69% of neonatal GBS disease would be prevented.[4] In January 1999, the Dutch Paediatric Association and the Society of Obstetrics and Gynaecology introduced guidelines based on the presence of risk factors. A risk factor based strategy was chosen as the estimated total incidence of proven and probable GBS sepsis in the Netherlands is relatively low (0.9 per 1000 live births) compared with the high incidence of proven GBS sepsis only in the USA before the introduction of the guidelines (1.1–3.7 per 1000 live births).[5]

The Dutch guidelines recommend antibiotic prophylaxis in the case of a previous infant with GBS disease, in heavily colonised mothers and in cases of intrapartum fever (>38.0°C). To limit the numbers of women receiving antibiotic prophylaxis, the guidelines recommend that in case of labour before 37 weeks or prolonged rupture of membranes (≥18–24 h), the woman should be first screened for GBS carriership, and antibiotic prophylaxis given if the culture is positive. The prophylactic antibiotics are given intravenously, with 5 million IU of penicillin G or 2 g amoxicillin given ideally 4 h before birth, followed by 2.5 million IU penicillin or 1 g amoxicillin, respectively, every 4 h until delivery. In case of delivery before the culture result is available, the obstetrician can give antibiotic prophylaxis based on their discretion (fig 1).[6]

The aim of the present study was to evaluate the incidence of GBS disease in the first three months of life during 1997–2001 in the Netherlands and to compare the incidence in the periods before and after the introduction of prevention guidelines.

METHODS

The ethics committee of the University Medical Centre Nijmegen approved the study.

We collaborated with the Dutch Paediatric Surveillance Unit (DPSU) for data collection. This unit coordinates an ''active'' case reporting structure to facilitate the investigation of uncommon paediatric diseases. Every month, the DPSU sends a card containing a variable menu of 10 conditions to all practising paediatricians in the Netherlands. During 1997–2001, neonatal GBS disease was included in the DPSU surveillance. Respondents were requested to report both proven and probable cases of GBS disease during the first three months of life, diagnosed in the preceding month. The DPSU forwarded the names of the reporting paediatricians to one of the authors (MTS). She then sent the paediatricians a questionnaire to collect clinical, microbiological and biochemical data on both mothers and infants.

As there was a possibility that the data reported to the DPSU might have been incomplete, the results were corrected for

Abbreviations: CFR, case fatality rate; DPSU, Dutch Paediatric Surveillance Unit; GBS, group B streptococci

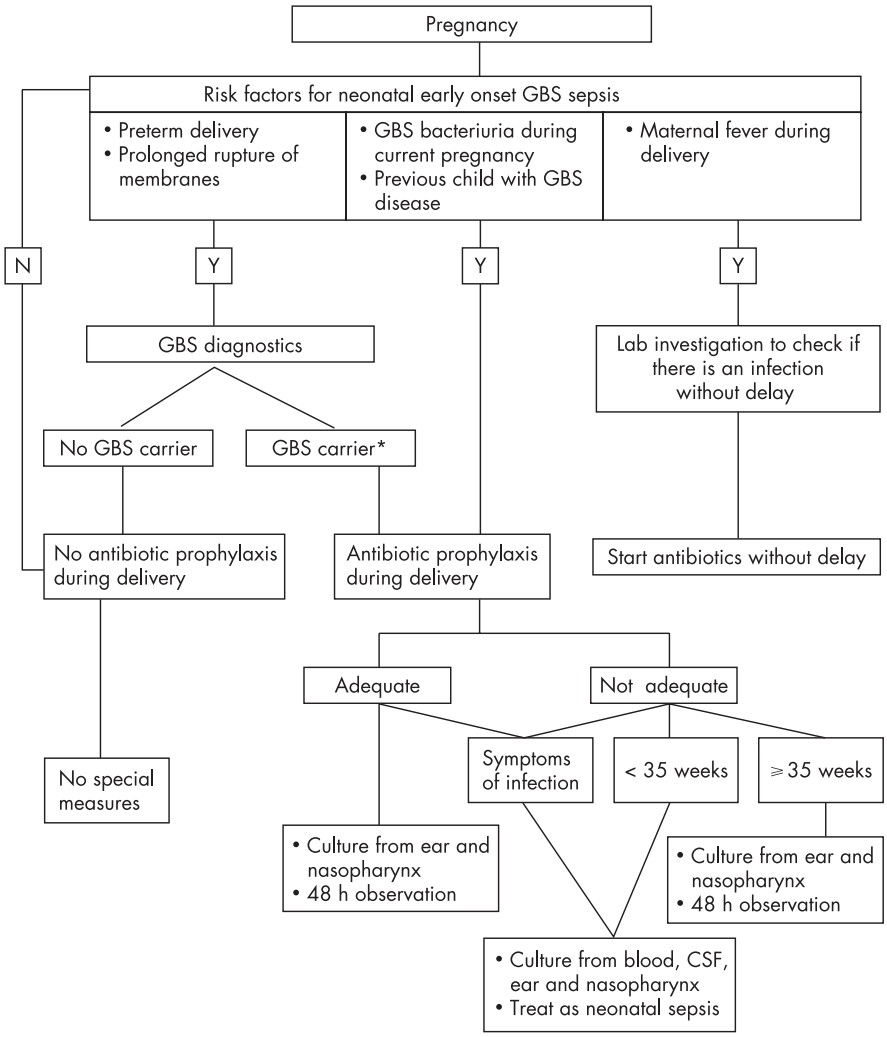

Figure 1 Prevention strategy of early onset group B streptococcal (GBS) disease in the Netherlands. *In case of delivery before the results of culture are ready, the obstetrician should decide about antibiotic prophylaxis based on the severity of the risk factor(s).

under-reporting. For this, we used the capture-recapture technique to estimate the number of cases missed by the DPSU surveillance. The technique uses numbers of cases reported to two independent sources. The corrected numbers of proven and probable cases can be calculated from the numbers reported by each source and the overlap between them.[7] The second independent source that we used was the response to a call for patients, published in a national parents' magazine, in which parents were asked to report to one of us (GdJ) if they had a child with GBS disease during the first three months of life in the years 1997–2001. We then checked whether the individual cases reported by parents had been reported to the DPSU by paediatricians. If not, relevant information was requested from the paediatrician involved. Finally, each case was classified as proven or as probable GBS sepsis or it was discarded, similar to the cases reported to the DPSU. We also estimated the level of completeness of reporting cases of GBS meningitis to the DPSU by the capture-recapture technique. Data from the microbiology laboratory at the Academic Medical Centre in Amsterdam, the national reference laboratory for bacterial meningitis, were used as the second independent source for data collection on cases of GBS meningitis.

To evaluate the relevance of the time between birth and the onset of the first symptoms of neonatal GBS infection we stratified the patients into three groups:

- very early onset (<12 h);
- late early onset (12 h – <7 days);
- late onset (7–90 days).

We analysed the data on neonates with proven and with probable GBS sepsis separately. The diagnosis of proven GBS sepsis was based on a positive GBS culture of blood and/or cerebrospinal fluid (CSF) along with presence of clinical features of septicaemia and abnormal results of laboratory investigations (leucocytosis or leucopenia, granulocytopenia, shift to the left, thrombocytopenia, elevated C-reactive protein). The diagnosis of probable GBS sepsis was based on the presence of the same clinical and laboratory features as for proven GBS sepsis and isolation of GBS from various sites, but without positive blood or CSF culture.[8]

Four obstetric risk factors of early onset GBS disease were documented: delivery before 37 weeks, ruptured membranes for ⩾18 h, intrapartum fever (>38.0°C) and previous delivery of a child with GBS disease.[9 10] The risk factor heavy maternal GBS colonisation (which may present as GBS urinary tract infection or GBS bacteriuria during the current pregnancy) was excluded from the analysis because in the Netherlands urine cultures are not routinely done.

We also collected data on sex, gestational age, parity, intrapartum antibiotic treatment, multiple pregnancies, mode of delivery, meconium staining of amniotic fluid, place of

delivery, exact age when first symptoms occurred, meningitis and fatal outcome. The effect of introduction of the guidelines on the incidence of GBS disease was expressed in terms of risk ratio (RR) and 95% CI. p Values <0.05 were considered to be significant.

RESULTS

Incidence of GBS disease

Over the whole study period (1997–2001) the corrected incidence of proven very early onset, late early onset and late onset GBS sepsis was 0.32, 0.11 and 0.14 per 1000 live births, respectively. The corrected incidence of probable very early onset, late early onset and late onset GBS sepsis was 1.10, 0.18 and 0.02 per 1000 live births, respectively.

Over the two-year period before the introduction of guidelines (1997–8), 642 cases of GBS disease were reported to the DPSU. Of these, 66 reports were excluded from the study because they were double reports. Another 198 reports were excluded because they were not about GBS and did not meet the inclusion criteria. Among the latter, 124 reports were of GBS colonisation without clinical features and two were of positive GBS blood culture with no clinical features of septicaemia (bacteriaemia). The remaining 378 reports were included in the study, of which 184 had proven GBS sepsis and 194 had probable GBS sepsis (table 1). In the three-year period after the introduction of the guidelines (1999–2001), 948 cases of GBS disease were reported to the DPSU. Of these, 72 were excluded from the study because they were double reports and 312 because they were incorrect and did not meet the inclusion criteria. Among the latter, 164 cases had GBS colonisation without clinical features. The remaining 564 cases were included in the study, of which 246 had proven GBS sepsis and 318 had probable GBS sepsis (table 1).

In 1997–8, parents reported 27 cases of proven and 22 cases of probable GBS sepsis. Of these, 19 with proven and 8 with probable GBS sepsis were also reported to the DPSU. Therefore, the DPSU captured only 70% of proven and 36% of probable GBS sepsis. In 1999–2001, parents reported 33 cases of proven and 51 cases of probable GBS sepsis. Of these, 27 with proven and 19 with probable GBS sepsis were also reported to the DPSU. Therefore, the DPSU captured only 82% of proven and 37% of probable GBS sepsis.

After correction for under-reporting, the decrease in the incidence of very early onset GBS sepsis from 0.38 per 1000 live births in 1997–8 to 0.28 per 1000 live births in 1999–2001 was not statistically significant (p>0.05; table 1). Total proven early onset GBS sepsis, on corrected for under-reporting, decreased significantly from 0.54 per 1000 live births to 0.36 per 1000 live births (p<0.05; table 1). There was no decrease in the corrected incidence of total probable early onset GBS sepsis (1.3 per 1000 live births and 1.4 per 1000 live births, respectively; table 1). In the small category of late onset GBS sepsis, there was no decrease in the corrected incidence of proven cases.

Incidence of GBS meningitis

In 1997–8 and 1999–2001, 29 and 57 patients, respectively, with proven GBS meningitis were reported to the reference microbiology laboratory. As 16 and 36 of these were also reported to the DPSU, the DPSU captured only 55% of GBS meningitis cases in 1997–8 and 63% in 1999–2001. Therefore, the corrected incidence of proven GBS meningitis in these two periods was 0.14 (95% CI 0.11 to 0.17) per 1000 live births and 0.17 (95% CI 0.15 to 0.19) per 1000 live births, respectively, and in the total five-year period it was 0.16 (95% CI 0.14 to 0.17) per 1000 live births. The proportion of patients with GBS meningitis was clearly related to the time of onset of GBS disease and increased from 6% if the onset was <12 h to 53% if the onset was ⩾7 days after birth (table 2).

Case fatality rate

In the whole five-year period, the case fatality rate (CFR) of proven early and late onset GBS sepsis was 8% and 5%, respectively. The CFR of proven early onset GBS sepsis was 7% versus 9% in the two periods and the mortality was similar (0.028 per 1000 live births). The CFR of proven late onset GBS sepsis was 7% in the first period and 4% in the second period (table 3). The CFR of probable early and late onset GBS sepsis was 2% and 0%, respectively.

Timing of onset of GBS disease

In 1997–8, in 70% (n = 128/184) of all patients with proven GBS sepsis reported to the DPSU and in 1999–2001, in 57% (n = 140) of all patients with proven GBS sepsis reported to the DPSU (n = 246), first symptoms were observed within 12 h after birth. In 85% (157/184) and 80% (196/246) of the cases, respectively, the first symptoms occurred within 7 days after birth.

Table 1 Corrected incidence of proven and probable neonatal GBS sepsis before (1997–8) and after (1999–2001) the introduction of guidelines for prevention of early onset GBS disease in the Netherlands

	DPSU reported cases		Corrected incidence* per 1000 live births (95% CI)		Risk ratio (min–max)†
	1997/98	1999/01	1997/98	1999/01	
Live births			391 851	608 665	
Proven GBS sepsis					
Early onset	157	196	0.54 (0.42 to 0.67)	0.36 (0.32 to 0.41)	0.67 (0.48 to 0.98)
Very early	128	140	0.38 (0.30 to 0.46)	0.28 (0.22 to 0.34)	0.74 (0.48 to 1.13)
Late early	29	56	0.13 (0.07 to 0.19)	0.09 ‡	0.69 (0.47 to 1.30)
Late onset	27	50	0.14 (0.07 to 0.27)	0.14 (0.06 to 0.23)	1.0 (0.22 to 32.9)
Probable GBS sepsis					
Early onset	190	313	1.3 (0.61 to 2.1)	1.4 (0.9 to 1.9)	1.08 (0.43 to 3.11)
Very early	159	257	0.99 (0.44 to 1.53)	1.1 (0.65 to 1.52)	1.11 (0.42 to 3.45)
Late early	31	56	0.4 (0.0 to 1.1)	0.3 (0.06 to 0.53)	0.75 (0.05 to 53.0)
Late onset	4	5	0.01	0.02 (0.0 to 0.04)	2.0 (0.0 to 4.0)

DPSU, Dutch Paediatric Surveillance Unit; GBS, group B streptococci.
*Corrected for under-reporting to the DPSU by using the capture-recapture technique; this may lead to discrepancies in the data.
†Minimum–maximum calculated with lowest and highest estimates of incidence.
‡No under-reporting for this category.

Table 2 Incidence of reported proven GBS meningitis in the Netherlands: 1997–2001

Reported to DPSU 1997–2001	No.	Lumbar puncture performed n (%)	Positive lumbar puncture n (%)	Proved meningitis (%)
Early onset	353	132 (37)	55 (42)	16
Very early	268	79 (29)	17 (22)	6
Late early	85	53 (62)	38 (72)	45
Late onset	77	47 (61)*	41 (87)	53

DPSU, Dutch Paediatric Surveillance Unit, GBS, group B streptococci.
*Cochran-Armitage test for trend with time of onset, p<0.0001.

Table 3 Case fatality rates of proved cases of group B streptococcal (GBS) sepsis (<3 months) in the past three decades

	GBS sepsis	
	Early onset	Late onset
Remington and Klein [11]*		
1982	55	23
1995	10–15	2–6
2001	5–10	2–6
The Netherlands (all hospitals)†		
1997–1998	11/157 (7)	2/27 (7)
1999–2001	17/196 (9)	2/50 (4)
1997–2001	28/353 (8)	4/77 (5)
The Netherlands (NICUs)†		
1977–1981[12]	13/21 (62)	4/5 (80)
1985–1993[13]	18/78 (23)	2/4 (50)
1994–1996[14]	21/66 (32)	3/7 (43)
1997–2001 (this study‡)	14/111 (13)	2/19 (10)

*Values are %.
†Values are n/N (%).
‡Case fatality rate in the same eight neonatal intensive care units (NICUs) in the Netherlands as in 1994–6.

Risk factors and characteristics of infants and mothers in proven and probable GBS sepsis

In patients with proven very early onset (<12 h) GBS disease, the presence of the risk factor preterm delivery was significantly lower in 1999–2001 (40/140; 29%) compared with 1997–8 (54/128; 42%) (p<0.05). The prevalence of the risk factors prolonged rupture of membranes, intrapartum fever and a previous child with GBS disease did not change during this time. Table 4 shows the patient characteristics over the period 1997–2001 because there were no differences between 1997–8 and 1999–2001.

Risk factors

The presence of the risk factor preterm delivery was two to five times higher in case of proven and probable GBS sepsis than in the Dutch population. In proven very early onset GBS sepsis only, the presence of prolonged rupture of membranes and intrapartum fever was about three times higher (table 4). In 46.7% of all infants with proven early onset GBS sepsis and in 34.1% of all infants with probable early onset GBS sepsis none of the four risk factors was present.

Sex

Of the 430 infants with proven GBS sepsis, 57% were boys and of the 512 infants with probable GBS sepsis, 300 (59%) were boys. In the general population, this is 51.1% (p<0.05). There was no sex differences between the GBS early and late meningitis groups nor between the early and late fatal cases.

Birth order

Of the 268 infants with proven very early onset GBS sepsis 171 (64%) were first borns and of the 415 infants with probable very early onset GBS sepsis 243 (59%) were first borns, compared with 47% in the general population (p<0.0001).

Other characteristics

None of the mothers of infants with proven late early onset sepsis received antibiotics during delivery. The proven very early GBS sepsis group had two times more cases of twins, caesarean section and meconium stained amniotic fluid than expected in the Dutch population. Most of the infants with proven and probable very early onset sepsis (85% and 87%, respectively) were born in hospital (table 4).

DISCUSSION

We found that the incidence (corrected for 77% response) of proven neonatal GBS sepsis during 1997–2001 was 0.56 per 1000 live births in the Netherlands. For probable GBS sepsis the incidence (corrected for 37% response) was 1.38 per 1000 live births. We collected data on infants with probable disease because most of them perhaps had GBS sepsis. Early onset disease is usually defined as the occurrence of first symptoms in the first seven days after birth. We considered it appropriate to subcategorise early onset GBS sepsis in ''very early onset'' (<12 hours) and ''late early onset'' (12 h – <7 days) because: (1) with this approach, we found that in 76% (268/353) of proven early onset cases, first symptoms occurred within 12 h; (2) the risk factor prolonged rupture of membranes occurred more frequently in the very early group; (3) the risk factor intrapartum fever was only present in the very early group (52 *v* 0 infants); and (4) mothers of infants with proven very early onset GBS sepsis were more often primigravid (64% *v* 46%). The difference in birth order may partly be due to the longer duration of the first delivery.[15] Furthermore, more infants with proven GBS sepsis were boys. Two other Dutch studies also described this sex difference.[12 14] In our study this male preponderance was restricted to the very early onset and late onset groups. Following the introduction of the guidelines, after correction for under-reporting, there was a significant decrease in the total incidence of proven early onset GBS sepsis, from 0.54 per 1000 live births (1997–8) to 0.36 per 1000 live births (1999–2001) (p<0.05; table 1). This can be partly explained by the increase in use of intrapartum antibiotic prophylaxis in the Netherlands from 1.0% of all deliveries in 1997 to 5.9% in 2000 after the introduction of the Dutch guidelines.[16] The incidence of late onset GBS sepsis remained unchanged, probably because of nosocomial acquisition of the infection.[17 18]

The overall effect of the Dutch guidelines is disappointing because of the limited decrease in the incidence of proven early onset GBS sepsis, and no decrease in mortality, incidence of meningitis and probable sepsis. In the USA, the incidence of proven early onset GBS sepsis was higher, varying between 1.1 per 1000 live births and 3.7 per 1000 live births before the introduction of the prevention guidelines. In one study the incidence dropped from 1.7 per 1000 live births in 1993 to 0.6 per 1000 live births in 1998[19] after the introduction of prevention guidelines in 1996 based on screening or on the presence of risk factors.[3] In 2002 the US guidelines recommended a strategy based only on screening[20] and the incidence of early onset GBS disease dropped further to 0.3 per 1000 live births in 2004.[21] We carried out a study in 1999 and found that the incidence of neonatal GBS disease in Europe varied from 0.5 per 1000 live births to 2 per 1000 live births.[2] A recent national study in the UK (2000–1) found the incidence of early onset GBS disease was 0.48 per 1000 live births but antibiotic prophylaxis was rarely used at the time.[22 23] The Dutch

Table 4 Prevalence of risk factors among and characteristics of mothers and infants with proved and probable group B streptococcal (GBS) sepsis (1997–2001)

	Very early onset GBS sepsis		Late early onset GBS sepsis		Late onset GBS sepsis		
	Proven n (%)	Probable n (%)	Proven n (%)	Probable n (%)	Proven n (%)	Probable n (%)	Dutch population*
Number	268	415	85	88	77	9	
Preterm delivery (<37 weeks)	94 (35)	124 (30)	17 (20)	10 (11)	30 (39)	3 (38)	7.6
Prolonged rupture of membranes (≥18 h)	91 (34)	19 (5)	14 (16)	4 (4.6)	9 (12)	0 (0)	10.8
Intrapartum fever (>38°C)†	52 (19)	18 (4)	0 (0)	3 (3)	2 (3)	1 (11)	5.7
Previous child with GBS disease	2 (1)	9 (2)	1 (0)	1 (1)	2 (3)	0 (0)	<0.17‡
No risk factor	109 (41)	131 (32)	55 (65)	41 (47)	37 (48)	4 (44)	>80
Male sex	158 (59)	247 (60)	41 (48)	47 (53)	45 (58)	6 (67)	51.1%
First born	171 (64)	243 (59)	39 (46)	52 (59)	28 (36)	2 (22)	47.0%
Twin	19 (7)	21 (51)	2 (2)	7 (8)	10 (13)	0 (0)	3.5%
Caesarean section	55 (20)	104 (25)	12 (14)	20 (22.7)	13 (17)	1 (11)	10.5%
Meconium-stained amniotic fluid	42 (16)	90 (22)	8 (9)	16 (18.2)	2 (3)	0 (0)	7.6%
Home delivery	20 (7)	24 (6)	21 (25)	6 (7)	15 (19)	2 (22)	± 30%
Hospital delivery	228 (85)	361 (87)	56 (66)	74 (84)	56 (73)	7 (78)	± 70%

*Best estimates from several sources (eg Statistics Netherlands, Prismant, Institute for Health Care Management).
†The risk factor intrapartum fever was often not reported in the medical record (60%).
‡The probability of having a previous child with early onset GBS is calculated by multiplying the rate of attack of 3 cases per 1000 live births by 55.2%, the percentage of multiparous infants.

guidelines are based on recognition of risk factors. To limit use of antibiotic prophylaxis during delivery, in case of labour before 37 weeks and/or prolonged rupture of membranes women are first screened and then given antibiotic prophylaxis if a positive culture is obtained. In case of delivery before the culture result is available, the obstetrician decides whether prophylaxis should be given.[5] Therefore, the Dutch guidelines can be expected to have limited effectiveness because in the setting of preterm labour and/or prolonged rupture of membranes cases can be missed as a result of delay in culture results. Furthermore, in about 40–50% of cases of early onset GBS sepsis no maternal risk factors are present[24] and it has been shown in the USA that the screening strategy is more effective than the risk factor based strategy.[25]

As meningitis occurs more often in late onset GBS disease and chemoprophylaxis is effective in preventing early onset GBS disease, our study found that the incidence of meningitis did not decrease over the study period. Moreover, there is under-reporting of meningitis because in unstable (preterm) newborns, lumbar puncture is often omitted.

The CFR of GBS disease has decreased dramatically in the past 25 years[26] and in proven neonatal GBS sepsis it was less than 10% in the present study. In a more selected (neonatal intensive care unit) population, the CFR of proven early onset GBS sepsis has decreased in the past 25 years from about 62% to about 13% (table 3). The decline in CFR of GBS sepsis may be attributed to improvements in neonatal care, antibiotic prophylaxis and change of the virulence of group B streptococci.[27] The CFR and the mortality of proven early onset GBS sepsis did not decrease further after the introduction of the guidelines, partly because the administration of antibiotics is primarily for prevention and not for treatment of the infant with early onset GBS disease. Of the 77 infants with proven late onset GBS disease, 31 were born before 37 weeks. This confirms that preterm delivery is the most important perinatal risk factor in late onset disease.[28]

Most of the patients with very early onset GBS sepsis and very early onset probable GBS sepsis were born in hospital (85% and 87%, respectively) in contrast with about 70% of all deliveries in the Netherlands. This may be explained by the fact that in the Netherlands, pregnant women with risk factors are usually referred to hospital. Fifty-six infants with proven GBS sepsis were born at home, and only in 9 (16%) of them was one of the four risk factors present.

What is already known on this topic

- After implementation of guidelines in the USA, the incidence of early onset GBS disease markedly dropped from 1.7 per 1000 live births in 1993 to 0.6 per 1000 live births in 1998.
- In 1999, only 4 of 29 European countries (Denmark, Norway, Spain and the Netherlands) had nationwide guidelines for prevention of neonatal GBS infection.

What this study adds

- This study provides nationwide epidemiological data on neonatal GBS disease.
- It also presents an evaluation of the effect of nationwide guidelines for prevention of neonatal GBS infection in the Netherlands.

Thus, due to the limited effectiveness of the Dutch risk factor based guidelines for prevention of neonatal GBS disease, we recommend that these guidelines should be changed.

ACKNOWLEDGEMENTS

We thank all the paediatricians who contributed to the data collection, and the Dutch Paediatric Surveillance Unit and the Reference Laboratory for Bacterial Meningitis at the Academic Medical Centre Amsterdam for invaluable help in collecting data.

Authors' affiliations

M Trijbels-Smeulders, L A A Kollée, Department of Paediatrics, University Medical Centre Nijmegen, Nijmegen, The Netherlands
G A de Jonge (retired), Oegstgeest, The Netherlands
P C M Pasker-de Jong, Department of Epidemiology and Biostatistics, University Medical Centre Nijmegen, Nijmegen, The Netherlands
L J Gerards, Department of Neonatology, Wilhelmina Children's Hospital, University Medical Centre Utrecht, Utrecht, The Netherlands
A H Adriaanse, Department of Obstetrics and Gynaecology, Medical Centre Alkmaar, Alkmaar, The Netherlands

R A van Lingen, Princess Amalia Department of Paediatrics, Division of Neonatology Isala Clinics, Zwolle, The Netherlands

This study was funded by Zorg Onderzoek Nederland (project no. 2200004) and by Stichting Group B Streptococcen, the Netherlands.

Competing interests: None.

REFERENCES

1 **Boyer KM**, Gotoff SP. Prevention of early-onset neonatal group B streptococcal disease with selective intrapartum chemoprophylaxis. *N Engl J Med* 1986;**314**:1665–9.
2 **Trijbels-Smeulders MAJM**, Kollée LAA, Adriaanse AH, *et al*. Neonatal group B streptococcal (GBS) infection: incidence and strategies for prevention in Europe. *Pediatr Infect Dis* 2004;**23**:172–3.
3 **Centers for Disease Control and Prevention**. Prevention of perinatal group B streptococcal disease: a public health perspective. *MMWR Recomm Rep* 1996;**45**:1–24.
4 **Rouse DJ**, Goldenberg RL, Cliver SP. Strategies for the prevention of early-onset neonatal group B streptococcal sepsis: a decision analysis. *Obstet Gynecol* 1994;**83**:483–94.
5 **Schuchat A**, Wenger JD. Epidemiology of group B streptococcal disease. Risk factors, prevention strategies and vaccine development. *Epidemiol Rev* 1994;**16**:374–402.
6 **Trijbels-Smeulders MAJM**, Adriaanse AH, Gerards LJ, *et al*. Prevention strategy for neonatal early-onset group-B-streptococcal (GBS) disease in the Netherlands. *Rev Med Microb*, 2003;**14**:35–9.
7 **Wittes JT**, Colton T, Sidel VW. Capture-recapture methods for assessing the completeness of case ascertainment when using multiple information sources. *J Chronic Dis* 1974;**27**:25–36.
8 **Gerdes JS**. Clinicopathologic approach to the diagnosis of neonatal sepsis. *Clin Perinatol* 1991;**18**:361–81.
9 **Bramer S**, Wijk van FH, Mol BW, *et al*. Risk factors for neonatal early-onset GBS-related disease. A case-control study. *J Perinat Med* 1997;**25**:469–75.
10 **Schuchat A**, Deaver-Robinson K, Plikaytis BD, *et al*. Multistate case-control study of maternal risk factors for neonatal group B streptococcal disease. The Active Surveillance Study Group. *Pediatr Infect Dis J* 1994;**13**:623–9.
11 **Remington JS**, Klein JO. *Infectious diseases of the fetus and newborn infant*, 5th edn. Philadelphia: WB Saunders Company, 2001.
12 **Gerards LJ**. Group B streptococci in the perinatal period. Thesis, Utrecht University, the Netherlands, 1985.
13 **Adriaanse AH**, Lagendijk I, Muytjens HL, *et al*. Neonatal early onset group B streptococcal infection; a nine-year retrospective study in a tertiary care hospital. *J Perinat Med*, 1996;**24**:531–8.
14 **Sprij AJ**, de Jonge GA. Group B streptococcal infection in eight tertiary care hospitals 1994–96, a retrospective study. *Tijdschr Kindergeneeskd* 1999;**67**:224–8.
15 **The Netherlands Perinatal Registry**. *Obstetrics in the Netherlands, trends 1995–1999*. The Netherlands Perinatal Registry, 2005.
16 **Trijbels-Smeulders M**. Group B streptococcal disease: effect of the Dutch guidelines for prevention. Thesis, Nijmegen University, the Netherlands, 2006.
17 **Anthony BF**, Okada DM, Hobel LJ. Epidemiology of the group B streptococci: maternal and nosocomial sources for infant acquisition. *J Pediatr* 1979;**95**:431–6.
18 **Boyer KM**, Vogel LC, Gotoff SP, *et al*. Nosocomial transmission of bacteriophage type 7/11/12 group B streptococci in a special care nursery. *Am J Dis Child* 1980;**134**:964–6.
19 **Schrag SJ**, Zywicki S, Farley MM, *et al*. Group B streptococcal disease in the era of intrapartum antibiotic prophylaxis. *N Engl J Med* 2000;**342**:15–20.
20 **Centers for Disease Control and Prevention**. Prevention of perinatal group B streptococcal disease: revised guidelines from CDC. *MMWR Recomm Rep* 2002;**51**:1–24.
21 **Gibbs RS**, Schrag S, Schuchat A. Perinatal infections due to group B streptococci. *Obstet Gynecol* 2004;**104**:1062–76.
22 **Heath PT**, Balfour G, Weisner AM, *et al*. Group B streptococcal disease in UK and Irish infants younger than 90 days. *Lancet* 2004;**363**:292–4.
23 **Kenyon S**, Brocklehurst P, Blackburn A, *et al*. Antenatal screening and intrapartum management of group B streptococcus in the UK. *BJOG* 2004;**111**:226–30.
24 **Lopez Sastre JB**, Fernandez Colomer B, Coto Cotallo GD, *et al*. Trends in the epidemiology of neonatal sepsis of vertical transmission in the era of group B streptococcal prevention. *Acta Paediatr* 2005;**94**:451–7.
25 **Schrag SJ**, Zell ER, Lynfield R, *et al*. A population-based comparison of strategies to prevent early-onset group B streptococcal disease in neonates. *N Engl J Med* 2002;**347**:233–9.
26 **Yagupsky P**, Menegus MA, Powell KR. The changing spectrum of group B streptococcal disease in infants: an eleven-year experience in a tertiary care hospital. *Pediatr Infect Dis J* 1991;**10**:801–8.
27 **Fleming KE**, Bohnsack JF, Palacios GC, *et al*. Equivalence of high-virulence clonotypes of serotype III group B Streptococcus agalactiae (GBS). *J Med Microbiol* 2004;**53**:505–8.
28 **Lin FC**, Weisman LE, Troendle J, *et al*. Prematurity is the major risk factor for late onset Group B Streptococcus disease. *J Infect Dis* 2003;**188**:26.